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Environment, dam, management: Factors influencing passive transfer of immunoglobulins to neonatal calves

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The bovine fetus has a type of placentation that does not permit contact between maternal and fetal blood and therefore does not permit passive transfer of immunoglobulins (Ig) from the mother to her fetus. The bovine calf is born agammaglobulinemic and depends on the intake of an adequate amount of maternal colostrum to provide antibodies and other immune factors that confer protective immunity against environmental pathogens from the early postnatal period until the third or fourth month of life. Many factors related to the calf, the environment, the dam and management can influence the passive transfer of Ig to neonatal calves (5, 9, 24, 46).

Inadequate intake of colostrum immediately after birth, whether in quantity or quality, results in partial or complete failure of passive transfer (FPT) of Ig, which has been considered the most important risk factor for morbidity and mortality in neonatal beef and dairy calves (5, 9, 14, 16, 22, 30, 36, 46, 47). Various methods

used to diagnose FPT have been reviewed by others (24, 30). The level of IgG in serum has been considered the most accurate method to diagnose FPT in calves. The range of values considered for failure are < 8 g/L for total failure, >8 but <10 g/L for partial failure, and >10 g/L for adequate transfer of IgG (30). Some authors consider only > 10 g/L for adequate transfer and <10 g/L for inadequate transfer of IgG (5, 9, 14, 15, 18, 22, 46).

Various studies have shown that the prevalence of FPT in dairy calves may be around 10-35% (24, 30, 46). One study from USDA reported that more than 40% of dairy heifer calves have < 10 g/L in serum in the first day of life (51). In beef cattle, around 11-31% of calves reportedly achieved < 8 g/L during the first day of life (16, 29, 36).

There are direct associations between FPT and presentation of disease (septicemia, diarrhea, pneumonia) and mortality in calves during the pre-weaning period. Some studies have shown that calves with FPT (< 8 g/L) are between 1.6 and 9.5 times more likely to become ill, and between 2.7 and 5.4 times more likely to die than calves with adequate passive transfer during the first months of life (16, 36, 37, 40).

At the same time the performance of calves that had FPT is decreased compared to calves with adequate transfer of Ig. The average weight at weaning for calves with adequate Ig transfer can be 6-34 lb more than calves with FPT (14, 16, 17, 36, 40). All of this leads to economic losses due to

reduced growth, suboptimal reproductive performance, treatment costs and death losses.

An adequate colostrum management program and the early detection and treatment of calves suspected of FPT is required to improve the pre-weaning health and performance of the young stock in dairy and beef herds. The following will discuss in depth the factors that influence the Ig absorption process and different management and product alternatives that producers have to prevent FPT in calves.

Immunoglobulin Absorption

Absorption of immunoglobulins and other macromolecules in the small intestine of the newborn calf is a short-term, non-selective process which is induced and also stimulated to close by feeding (45, 49). The small intestinal absorptive cells in the neonate are induced to absorb macromolecules like immunoglobulins, other proteins like albumin and casein, and even microorganisms like E.coli, by pynocytosis once they have contact with any feed after birth. This process is non-selective, with each type of macromolecule having the same opportunity to be absorbed, therefore competing with Ig for receptors or binding sites in the enterocytes (45, 46). Once inside enterocytes the proteins absorbed are transported by vacuoles through the cytoplasm to the basal membrane and from there to lymphatics and the portal system where they enter the general circulation. Absorption of proteins

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seems to be higher in the jejunum than in the other portions of the small bowel (46). The cessation of the absorptive capabilities of the enterocytes is stimulated by feeding, especially by any protein (immunoglobulin, albumin, casein) in the feed. It seems that protein can activate an enzymatic digestive process in the cell that breaks down the vacuoles involved in transportation, thus impeding the process (45, 46, 47, 48). Other factors like maturation of small intestine cells, increased abomasal acidity, and development of intestinal secretions (digestive enzymes) could be involved in the cessation of absorption of Ig (45).

Therefore the efficiency of IgG absorption depends on the time of first colostrum feeding, the concentration of IgG in the colostrum, and the total amount of colostrum fed per unit of body weight (9). Some authors have established a formula to calculate an Apparent Efficiency of Absorption (AEA) of IgG in calves as follows: $AEA = \text{plasma IgG at 24 h (g/L)} \times \text{Body Weight (kg)} \times 0.092 / \text{total IgG intake in grams (13)}$. The average of AEA IgG level is around 20 to 35% (13, 44, 50).

Factors influencing the passive transfer in calves

Many factors have been established to affect the absorption of IgG in neonates, but the age (in hours) at first ingestion of colostrum, the concentration of IgG in the colostrum ingested, and the total amount of colostrum at first ingestion are the primary influencing factors.

Once enterocytes come in contact with feed (protein) the closure process begins. Some research has stated that the first 4 hours of life are the most critical period to absorb large quantities of Ig, and that after only 8-12 hours of life the absorption capacity is severely diminished. (27, 28, 46). Even if the calf has not been fed, a spontaneous closure (cessation of uptake of macromolecules by intestinal cells) occurs by 24 hours of life (46).

There is also evidence that the higher the concentration of IgG in colostrum, the higher its absorption (12, 14, 22). There are major differences in colostrum IgG concentration between cows. A primary factor influencing IgG concentration is breed, with dairy breeds with higher total milk volume at first milking typically having a lower Ig concentration per unit

of colostrums than other breeds with lower total volume at first milking (12, 14, 22, 39, 46, 47, 53). Some authors have stated that the colostrum of younger cows and first-calving heifers has lower IgG concentration than colostrum from older cows (30, 37, 39). Similarly, calf serum IgG concentrations have been found to increase as the dam's age increase, reaching a maximum level at the 3rd or 4th calvings (34, 36, 37, 53).

Differentiating a high IgG concentration colostrum from low concentration colostrum is problematic (53). Because colostrum is also composed of other proteins, lipids, carbohydrates, minerals, hormones, growth factors and cells besides Ig, the Ig / total solids ratio becomes important because the higher the concentration of Ig the higher its potential for absorption (46, 47, 22, 48, 22, 23, 24). A lower ratio of Ig / total solids increases the competition for absorptive binding sites in the small intestine and the efficiency of absorption of Ig will be diminished.

Some works have shown that the natural act of suckling compared with bucket, nipple bottle or esophageal tube administration of colostrum enhances and increases the efficiency of absorption of Ig. This appears to be related to a larger amount of colostrum being consumed by the calf and also to the closure of the esophageal groove stimulated by suckling that favors Ig reaching the absorptive cells in the intestine more rapidly (48, 36, 24).

Conversely, some authors have shown high rates of FPT in dairy calves that are left with the dam and allowed to suckle naturally (1, 9), the explanation being that suckling dairy calves consume less concentrated colostrum. It is important to state that many times if the quality of colostrum is low ($< 50 \text{ g/L IgG}$) the administration of 2 L of colostrum is probably insufficient to achieve adequate Ig transfer to calves. For that reason it is important to promote adequate suckling or ensure feeding of a sufficient amount of colostrum to reach the targeted quantity of Ig consumption during the first 4 hours of life.

Other factors like dystocia, environmental temperature, factors associated with the pre-partum period and nutrition management of the dam have been related with FPT (12, 34, 36, 43).

Dystocia or delayed parturition has been reported to diminish passive transfer of Ig to calves. Hypoxemia in the dystocic calf affects the absorptive capability of the small intestine (36, 53, 18). Also, affected calves sometimes have problems related to inability to stand and suckle (15, 36). Some studies have found intestinal lesions in neonatal calves that have suffered a prolonged dystocia, resulting in impairment in the absorptive capabilities of the enterocytes (26).

The environmental temperature the day of calving may influence the absorption of Ig. Some works have shown that high temperatures or "heat stress" decrease the rate of absorption of Ig (49, 15). Similarly, low temperatures or cold stress can negatively affect the rate of absorption because hypothermia decreases the blood flow to the small intestine and diminishes absorption capability of enterocytes (35, 15, 18, 21).

Another factor implicated has been the pre-partum nutrition of the dam. Some work has shown that the concentration of Ig in colostrum is 50% lower in overconditioned beef cows compared with properly conditioned beef cows (43). Other work has indicated that increased body condition score (>5) in first-calf beef heifers is associated with increased IgG levels in calf serum (34). Calves born to cows with poor udder conformation or a history of mastitis also should be categorized as high risk for FPT (37, 52).

Alternatives for prevention of failure of passive transfer:

Ongoing problems with FPT have created a renewed emphasis on colostrum-management programs and caused producers to look for alternative solutions such as colostrum supplements or colostrum replacers to provide passive immunity to neonatal calves.

Other on-farm colostrum

A common practice on some dairy and beef farms, and considered to be the best option, is the utilization of fresh or pre-collected frozen colostrum as the primary source of passive immunity to the calf. The objective is to offer an adequate amount of excellent quality colostrum shortly after birth. Since parity and lactation level can influence the colostrum

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concentration of Ig, it is important to always harvest the initially-available colostrum and determine whether it has sufficient Ig concentration to meet the needs of the calf. It is considering good quality colostrum when it has IgG levels > 50 g/L. An acceptable on-farm method to measure the IgG concentration is the use of a colostrometer or hydrometer to check the colostrum density. Some works have shown that a colostrum density > 1050 correlates with > 50 g/L of IgG (4, 38, 44).

The general recommendation is to administer about 200 g of IgG totally to achieve > 10 gr of IgG in the calf's blood; therefore, approximately 4 L of 50 g/L colostrum should be administered during the first 4 hours of life (19, 24, 44).

Maternal or on-farm pooled colostrum provides other nutrients and beneficial components in addition to its role as a source of IgG. Carbohydrates, fat, minerals, growth factors, cytokines, lactoferrin, and viable leukocytic cells are present in natural colostrum and play an important role in the development of immunologic capabilities of the neonate. It also provides specific antibodies against common on-farm and environmental pathogens, as well as vaccines to which the dam has been exposed, making it more effective in protecting the calf (4, 41, 50, 54).

Colostrum supplements and colostrum replacers

In cases of absence of the mother, poor colostrum quality, little frozen colostrum reserve or high resident herd incidence of potentially colostrum-transmitted infectious diseases such as Johne's Disease, Bovine Leukosis Virus (BLV), Salmonellosis, etc., producers may choose to use colostrum supplements or replacers to provide exogenous sources of IgG (13, 16, 24, 44).

Colostrum supplements and replacers are commonly derived from bovine lacteal secretions (milk whey or colostrum), eggs, bovine serum or from concentrated IgG from bovine plasma, all of which are available commercially (with the exception of products derived from concentrated IgG from bovine plasma). The IgG provided by these products are not specific against the common farm pathogens, but can provide generic protection against several key pathogens. Research studies done with these products show variable results – some works show an acceptable transfer of

immunoglobulins to calves (13, 19, 25, 40, 42, 44), while other commercial products tested did not provide adequate IgG transfer (4, 32, 33, 41, 54).

Factors like source of IgG, method of fractionation of IgG, non-Ig protein concentration, IgG/total solids ratio and inability to provide viable leukocytes, growth factors, cytokines and lactoferrin may affect the efficiency of absorption of colostrum supplements/replacers and may impair their ability to provide adequate immune transfer (13, 24, 33, 44, 46). Some authors have shown a decrease in live animal performance when maternal colostrums-fed calves were compared with colostrum supplement-fed calves (25).

Colostrum supplements

The colostrum supplements are commonly derived from whey and cow colostrum and usually contain very low concentrations of IgG per dose, usually 17-50 g IgG. They are not recommended to replace colostrum, but are recommended to mix with and improve low-quality colostrum (24). Generally the non-IgG protein concentrations of these products are very high and the ratio of IgG/total solids is very low. Many studies have shown a decreased efficiency of absorption of Ig when colostrum supplements are administered alone or when mixed with maternal colostrum (13, 15, 24, 32, 33, 41, 4). However, a few studies have shown adequate passive transfer with the use of colostrum supplements (5).

Many works have shown that the low amount of IgG compared with the high non-Ig protein and total solids present in these products compete and interfere with the efficiency of Ig absorption in the small intestine in the neonate (13, 41, 54). Also the addition of more colostrum supplement or the administration of two doses to increase the amount of IgG offered to calves decreases the efficiency of absorption even more. Some works have shown that this practice can reduce the Apparent Efficiency of Absorption (AEA) in 37% of calves so treated (13, 24). Reportedly the addition of bovine serum albumin to maternal colostrum reduced serum IgG concentration in newborn calves from 9.3 to 6.9 g/L (8).

Other work has shown that colostrum supplements as a single dose feeding or as a mixture with colostrum never achieve 10 gr of Immunoglobulin G in serum of

neonatal calves after 24 hours of life and that the average daily gain from 0-3 weeks of life is about 175 g/day less for the colostrum supplement-fed calves (32).

Some colostrum supplements derived from hyperimmunized chicken eggs containing immunoglobulin Y have shown low intestinal absorption in the calf and also a low levels in circulation.

Colostrum replacers

Colostrum replacers normally are derived from bovine serum or from IgG concentrates from plasma, and usually contain > 100 g of IgG per dose. These products are formulated to replace colostrums. Some studies have shown that colostrum replacers derived from concentrated IgG from bovine plasma can achieve high levels of IgG in newborn serum (13, 19, 40, 42). The explanation for the improved efficiency of absorption for colostrum replacers compared with colostrum supplements are the source and the concentration of IgG present in these products.

Some studies utilizing bovine serum-derived colostrum replacers have shown that a single dose will not achieve > 10 g of IgG in serum of neonatal calves, and that doubling the initial dose will further reduce the efficiency of absorption (40). This is possibly due to the effects of increase total solids and non-Ig protein in the total mass of product and its interference with the absorption process in the small intestine (4).

Other studies have used a non-commercially available, concentrated IgG product derived from bovine plasma, and reported adequate transfer of immunoglobulins with a single dose, and also an increase in the serum level of IgG from 11.6 to 13.6 g/L with a second dose of the product (50). These findings indicate that the colostrum replacers derived from concentrated IgG from bovine plasma are effective in preventing FPT in calves (13, 19, 25, 40, 42).

The most recent studies testing commercially-available colostrum replacers under field conditions have shown that they are not effective in achieving adequate serum levels of IgG in newborn calves, and in one of these studies 93.1% of the calves were considered FPT (< 10 g/L IgG) compared with maternal colostrum-

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fed calves. The consumption of roughly 170 g of IgG in the colostrum replacer was able to increase the serum IgG level only to 8 g/L on average (44, 50).

In various studies where colostrum replacers or colostrum supplements have been utilized, there have not been significant differences in the presentation of disease, frequency of treatments or mortality rates between calves fed these products when compared to maternal colostrum (32, 44, 50). It is possible that the total IgG level achieved by these products provide some degree of protection from disease. It is also possible that the calf's level of exposure to challenge microorganisms in these trials have been reduced.

Conclusions

The absorption of immunoglobulins by the newborn calf is a complex, nonselective process that can be influenced and affected by many factors; the most important of which are the amount and concentration of IgG in colostrum and the time at first feeding. The most effective method to prevent failure of passive transfer in calves is a colostrum-management program that assures the adequate amount of colostrum intake during the first 4 hours of life by promoting suckling or force feeding. The use of colostrum supplements or replacers should be restricted to special or emergency circumstances when maternal or on-farm colostrum is not available, and then a product with a high concentration of IgG must be selected. Additional research is needed to identify the interactions between the colostrum supplements and replacers and the absorptive process in the intestine to get a truly workable solution for the problem.

Factors like dystocia and environmental temperature (heat or cold stress) have to be considered as they increase the risk for failure of passive transfer. A good dam nutrition and vaccination program can also help to prevent the condition in neonatal dairy and beef calves.

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Vaccination debate prompts new strategies for dogs, cats

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Within the last decade, the frequency of small animal vaccinations, the efficacy of certain vaccines and the patient's need for various vaccines has become a topic of considerable debate. The impetus for the discussions was emerging evidence linking vaccines with fibrosarcomas in numerous cats. The ripple effect quickly spread to include dogs in the discussions although there was less specific evidence of long-term vaccine associated diseases in that species.

The increasing number of non-core, novel vaccines in the marketplace fueled over-vaccination concerns. The ensuing vaccine-related concerns have focused on the necessity of routine annual vaccines in adult dogs and cats combined with mounting evidence that vaccines can cause serious systemic diseases in both species.

Vaccinations are an important part of maintaining a healthy animal, however vaccine risk awareness, cost factors, antigen overload considerations, and regional disease incidences now require the owner and veterinarian to make rational and balanced vaccine selection decisions based on risk assessment of each patient. Among vaccine experts in academia, the trend has been to promote the concept of vaccine risk assessment for each patient, i.e. every patient does not automatically need every vaccine every year. Not surprisingly, many of the biological manufacturers have not endorsed or embraced this idea.

Allergic reactions to vaccines are relatively rare. Reactions occur as a result of an immediate or delayed hypersensitivity reaction to the antigenic component(s) of the vaccine. In addition, vaccine suspensions also may contain allergic components associated with production methodology that may include proteins from tissue culture or egg yolks. The allergic reaction also can occur from the antibiotics or preservatives present in the vial.

Allergic reactions can result in milder symptoms (localized swelling, systemic signs of depression, vomiting and/or diarrhea), to severe systemic shock and possible death. In addition to the more

obvious vaccine-induced allergic reactions is the less definitive group of systemic diseases that have also been postulated as being linked to vaccines. Unlike allergic reactions, the cause and effect of various canine vaccines with these diseases are less clear-cut, and the scientific basis for the relationship is often anecdotal.

Unfortunately the duration of immunity for each vaccine is a complex issue involving the particular antigen used, for example, MLV vs. killed agent; various manufacturing techniques including the adjuvant used; the individual patient's response to the vaccine, age of the patient, and previous vaccine history.

Traditionally, veterinarians have relied on vaccine manufacturers to provide the duration of immunity (DOI) data to the profession. Ironically the one-year re-vaccination recommendations for most canine and feline vaccines were not determined by a scientifically validated study. Except for rabies vaccination, we don't know the exact duration of immunity for most current canine vaccines produced because most DOI studies are based only on one-year serum titers extrapolations and not on timed experimental challenge.

Fortunately in the last four years, several companies have accepted the challenge of developing and gaining USDA approval of canine and feline three-year duration of immunity core vaccines. These vaccines have demonstrated both protective titers at three years post vaccination, and animals have withstood pathogenic viral challenges at three years post vaccination.

Although many veterinary clinics still recommend annual re-boosting to protect against the core diseases, the more progressive practices are now employing a three-year re-booster schedule advocated by most veterinary teaching hospitals, the AVMA, and recently the American Animal Hospital Association (AAHA). The basis for changing the traditional annual vaccine protocol recommendations to three-year programs and eliminating unnecessary vaccine was based on the premise that active immunization to most viral antigens probably persists for several years or perhaps even throughout the life of the patient. Arguably Leptospirosis,

Corona virus, Giardia, Lymes, and Bordetella vaccines are good for one year, if that long.

Selected Reading

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Winter hay feeding practices affect stable fly numbers

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It's time to remind cattlemen that stable flies attacking pastured cattle this spring and summer may have come from sites where round hay bales were fed to cattle during the winter. Over the last three decades there has been a dramatic increase in the population of these blood-sucking flies.

Formerly a major pest of livestock in confined-feeding operations such as dairies and feedlots, stable flies have extended their host range to attack pastured and range cattle. Cattle waste up to 50% of the hay when feeding on round bales. Mixed with cattle feces, wasted hay develops into an ideal habitat for stable fly larvae. As a result, stable fly populations reach major

damaging levels for about 8 weeks during spring and early summer and can cause a loss of 0.5 lb/head/day. Lower fly densities before and after this period also detrimentally affect cattle performance. Recent estimates of of stable flies' combined economic impact on dairy and pastured and confined beef cattle production show it to be greater than \$2 billion a year in the United States.

There is no effective method for controlling stable flies attacking pastured and range cattle. Cultural methods that reduce larval media by decreasing the amount of wasted hay at the round bale feeding site are recommended. Suggestions include the following:

- Use a hay feeding ring rather than placing the bale on the ground.

- Use cone feeders, which have a demonstrated ability to reduce the amount of wasted hay.
- Move hay feeders frequently to prevent accumulation of the hay-manure medium in one spot over time.
- Unroll the round bales on pastures, changing sites each time.
- Spread accumulated hay-manure medium to allow it to dry out.

Although stable flies are good fliers capable of dispersing up to 155 miles on prevailing winds, population levels pestering a given herd depend on the number of flies emerging from round bale feeding sites in the vicinity. Cultural methods may not be effective if neighboring ranches do not prevent the development of large populations of stable flies on their premises.

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May 27-28, 2009

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March 21

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March 21

South Central Goat Conference, Lyons

April 17

Kansas Wildlife Habitat Evaluation Contest, Burlington

April 18

High Plains Horseman's Day, Oakley



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